



RESEARCH ARTICLE

CLINCO PATHOLOGICAL STUDY OF BRONCHIAL BIOPSIES: A PROSPECTIVE STUDY FROM A TERTIARY CARE HOSPITAL IN KASHMIR VALLEY

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ABSTRACT

Background: Lung cancer is currently the most frequently diagnosed major cancer in the world and the most common cause of cancer mortality worldwide. It comprises about 17% of the total new cancer cases in males and 23% of the total cancer deaths. The incidence is increasing dramatically in women and lung cancer has surpassed breast cancer as a leading cause of cancer death in women. To combat the disease successfully, lung cancer should be diagnosed at earliest possible stage preferably before the lesion has reached the stage of a visible and palpable tumor.

Aim: To study the role of bronchial biopsies in diagnosis of different lung lesions, study the correlation between various histopathological lesions of lung with age and sex of patients and to find correlation between clinical presentation and nature of lung lesions.

Materials and Methods: Two year prospective study conducted in the Department of Pathology Government Medical college Srinagar, from July 2013 to August 2015. The study was conducted on 130 bronchial biopsies including transbronchial biopsies (TBB). The biopsies so obtained have been fixed in 10% buffered formalin. And the specimen of tissue have been processed, then sections of 4-5 micron thickness have been prepared and stained with routine hematoxylin and eosin.

Results: In our study conducted on 130 bronchial biopsies (including TBB), the results are summarized as under. Out of a total of 130 clinically suspected cases of lung cancer tumor was found in 83 cases (83/130) by biopsy. The overall mean age of patients of primary lung cancer was 63.12 years with maximum number of cases seen between 61-70 years. The mean age for men was 62.23 years and for females, it was 59.34 years. The peak incidence of the disease was seen in age group of 61-70 years which constituted 32.03% percent of all cases. Minimum age was 35 year old male diagnosed as well differentiated squamous cell carcinoma, maximum age seen was 90 years. Males were more common affected by lung tumors than females with a male to female ratio was 1.88:1. Tumor was found in the right side of lung in 58 cases (69.87%) and in the left side of lung in 25 cases (30.12%). The smoker to non-smoker ratio was 1.4:1. The two main histological sub-types of lung cancer among smokers was squamous cell carcinoma (65.06%) and Adenocarcinoma (19.27%). Diagnostic yield for endobronchial biopsy was 63.84% (83/130 cases), Squamous cell carcinoma (65.25%) and small cell carcinoma (12.4%) were more associated with endoscopically visible lesions than other cell types. Adenocarcinoma and (54%) and large cell carcinoma (57%) were more associated with peripheral lesions. Squamous cell carcinoma, Adenocarcinoma, small cell carcinoma are more common in males whereas Pleomorphic anaplastic carcinoma was seen exclusively in females.

Conclusion: The bronchial biopsies permits exact diagnosis of specific entity histologically including infectious pathology at earliest stage. Thus in the present study yield of diagnosis was highest with the bronchoscopic biopsies and in maximum number of cases, specific histopathological diagnosis was made on biopsies only.

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INTRODUCTION

Lung cancer is currently the most frequently diagnosed major cancer in the world and the most common cause of cancer mortality worldwide. (Brambilla et al., 2001) It comprises about 17% of the total new cancer cases in males and 23% of

the total cancer deaths. (Jemal et al., 2011) The incidence is increasing dramatically in women and lung cancer has surpassed breast cancer as a leading cause of cancer death in women. Overall lung cancer is most frequent fatal malignancy. (Brambilla et al., 2001; Hussain Aliya, 2010) Nearly 70 per cent of all new cases of lung cancer in the world occur in developed countries (Parkin et al., 1988) but incidence is rising at an alarming rate in developing countries also. (Parkin, 1989) Cancer of the lung most often occurs between age 40 and 70

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years with a peak incidence in the fifties and sixties. Only two percent of all cases appear before the age of 40. (Jemal *et al.*, 2011) Approximately 80-85% of lung cancer deaths are attributed to smoking. (Wingo *et al.*, 1999; The Health Consequences of Smoking, 2004) Estimates of the relative risk of lung cancer in the long-term smoker compared with the lifetime nonsmoker vary from 10- to 30-fold. The cumulative lung cancer risk among heavy smokers may be as high as 30 percent, compared with a lifetime risk of lung cancer of 1 percent or less in never smokers. (Samet, 1991; Samet *et al.*, 1988) The risk of bronchogenic carcinoma is proportional to the total lifetime consumption of cigarettes. The relative risk increases with both the number of cigarettes smoked per day as well as the lifetime duration of smoking. (Mattson *et al.*, 1987) Additional factors include age at onset of smoking, degree of inhalation, tar and nicotine content of the cigarettes use of unfiltered cigarettes. (Harris *et al.*, 1982; Loeb *et al.*, 1984) Besides smoking other occupational and environmental carcinogens which increase the increase the risk of lung cancer include asbestos, radon, arsenic, bis-chloromethyl ether, chromium, formal-dehyde, ionizing radiation, nickel, polycyclic aromatic hydrocarbons, hard metal dust, and vinyl chloride. (Chen *et al.*, 2004) The role of genetic factors as a cause of lung cancer is only poorly understood, but increasing evidence suggests that such factors play a role. A number of studies suggest that first-degree relatives of individuals with lung cancer have an increased risk of developing lung cancer. (Matakidou *et al.*, 2005; Cote *et al.*, 2012) Non-smokers account for 15% of lung cancer cases, and these cases are often attributed to a combination of genetic factors, radon gas, asbestos, air pollution and passive smoke. (Sun *et al.*, 2007) Signs and symptoms associated with lung cancer depend on tumor location and extent, as well as tumor biology. (Chute *et al.*, 1985; Patel and Peters, 1993) Central tumors arising in larger airways usually cause cough, sputum production, wheezing, or hemoptysis. Peripheral tumors can cause cough, dyspnea, and chest pain that may be confused with angina. (Patel and Peters, 1993) To combat the disease successfully, lung cancer should be diagnosed at earliest possible stage preferably before the lesion has reached the stage of a visible and palpable tumor. (Beckles *et al.*, 2003)

Aims and Objectives

1. To study the role of bronchial biopsies in diagnosis of different lung lesions.
2. To study the correlation between various histopathological lesions of lung with age and sex of patients
3. To find correlation between clinical presentation and nature of lung lesions.

MATERIALS AND METHODS

Two year prospective study conducted in the Department of Pathology Government Medical college Srinagar, from July 2013 to August 2015. The study was conducted on 130 bronchial biopsies including transbronchial biopsies (TBB))

Inclusion criteria

All bronchial biopsies received at our department.

Exclusion criteria

Inadequate biopsies.

Methods of collection of data

The study included bronchial biopsies performed at CD hospital one of the associated hospitals of GMC Srinagar during the period of August 2013-July 2015. Brief clinical data have been noted from the case records which include the age and sex of the patient, relevant history if any, presenting clinical and radiological diagnosis. The specimens so obtained have been fixed in 10% buffered formalin. And the specimen of tissue have been processed, then sections of 4-5 micron thickness have been prepared and stained with routine hematoxylin and eosin.

RESULTS AND OBSERVATION

This was a two year Prospective study conducted in the Department of Pathology Government Medical college Srinagar, from July 2013 to August 2015. The study was conducted on 130 bronchial biopsies (including transbronchial biopsies (TBB)).

Table 1. Sex wise distribution of cases

Category	No. of cases	Percentage of cases
Males	85	65.38%
Females	45	34.61%
Total	130	100%

Table 2. Age and sex wise distribution of cases

Age group	Males	Females	Total	Percentage
31-40	2	2	4	3.07%
41-50	12	8	20	15.38%
51-60	22	11	33	25.38%
61-70	35	18	53	40.76%
71-80	11	5	16	12.30%
>81	3	1	4	3.07%
Total	85	45	130	100%

Table 3. Smoking History

Sex	Cigarette smokers/hokkah smokers	Non smokers	Total
Male	72	13	85
Female	4	41	45
Total	76	54	130

Table 4. Various histological type of lung malignancies among smokers and non smokers

Diagnosis	No of Cases	Smokers		No. of cases	Nonsmokers	
		M	F		M	F
Squamous cell carcinoma	37	35	2	17	8	9
Adenocarcinoma	12	11	1	4	1	3
small cell carcinoma	5	4	1	5	3	2
Undifferentiated carcinoma	1	1	0	1	1	0
Pleomorphic anaplastic carcinoma	0	0	0	1	0	1
Total	55	51	4	27	13	14

Table 5. Histopathological findings found on biopsy

Histopath.dx	Males	%	Females	%	Total	%
Squamous cell carcinoma	43	67.18%	11	57.89%	54	65.06%
Adenocarcinoma	12	18.75%	4	21.05%	16	19.27%
Small cell carcinoma	7	10.93%	3	15.78%	10	12.04%
Undifferentiated carcinoma	2	3.12%	1	5.2%	3	3.61%
Total	64	100%	19	100%	83	100%

Table 6. Clinical symptoms in different lung tumors

Histological type	Cough	Hemoptysis	Fever	Shortness of Breath	Hoarsness of Voice	Weight loss
Squamous cell carcinoma	23	8	11	7	3	6
Adenocarcinoma	9	3	4	3	5	4
Small cell carcinoma	6	3	5	2	5	2
Undifferentiated Large Cell Carcinoma	2	1	-	-	-	-

Table 7. Histopathology of Benign Cases on Bronchial Biopsy

Histopathology	benign positive cases on BB	
	M	F
Tuberculosis	4	2
Chronic inflammatory Pathology	15	14
Squamous metaplasia	2	10
Total	21	26

Table 8. Clinical Symptoms in Benign Lesions

Histopathology	Cough	Hemoptysis	Fever	Shortness of Breath	Weightloss
Chronic inflammatory pathology	11	3	7	4	6
Squamous Metaplasia	7	0	4	0	4
Tuber culosis	3	0	2	2	2

Table 9. Benign Cases According to Sex Distribution

Category	No. of cases	Percentage of cases
Males	21	44.6%
Females	26	55.3%
Total	47	100

Table 10. Male to female ratio of malignant lesions in different studies

Category	Fuladi <i>et al</i> (2004)	Koul <i>et al</i> (2010)	Sheema <i>et al</i> (2010)	Our study
Male to Female ratio	6.22:1	6.1:1	6.98:1	3.36:1

Table 11. Comparative clinical features and cell type pattern in different Indian Studies

Authors	Jindal <i>et al.</i> (1990)	Chokhani, (1998)	Koul <i>et al.</i> (2010)	Sujit Kumar <i>et al.</i> (2011)	Our study, (2015)
Age group predominantly affected	54.3	61	55.77	-	60.78
Male to Female ratio	-	2.8	6.1:1	6.6:1	3.36:1
Smokers/Non Smokers ratio	2.7	7.3	4.54:1	4.31:1	1.40:1
Squamous cell carcinoma	34.3%	64%	67.5%	35.34%	65.06%
Small cell carcinoma	27.8%	22%	20.8%	13.91%	12.04%
Adenocarcinoma	25.9%	8%	3%	15.79%	19.27%
Large cell carcinoma	-	1%	1.08%	1.55%	3.6

DISCUSSION

Lung cancer is the leading cause of cancer related deaths in men and in women it has surpassed even breast cancer. (Jemal *et al.*, 2011) The increase number of the lung cancer deaths is mainly because it is detected at a late stage. Timely detection of disease plays a important role in the management and long term survival of patients. (Prasad *et al.*, 2006) Histopathology is valuable tool in the diagnosis of lung malignancies. Fibreoptic bronchoscopy was introduced in 1968 as a diagnostic procedure

(Basu and Ghosh, 1971). Since then apart from sputum, different methods for obtaining satisfactory specimens have become available. The present study was therefore undertaken to ascertain the role and diagnostic utility of bronchial biopsy in diagnosing and subsequent management of patients with bronchogenic carcinoma.

The present study included 130 clinically suspected cases of lung malignancies. The study included only those cases where bronchial biopsy (including TBB) was done.

Photo micrographs

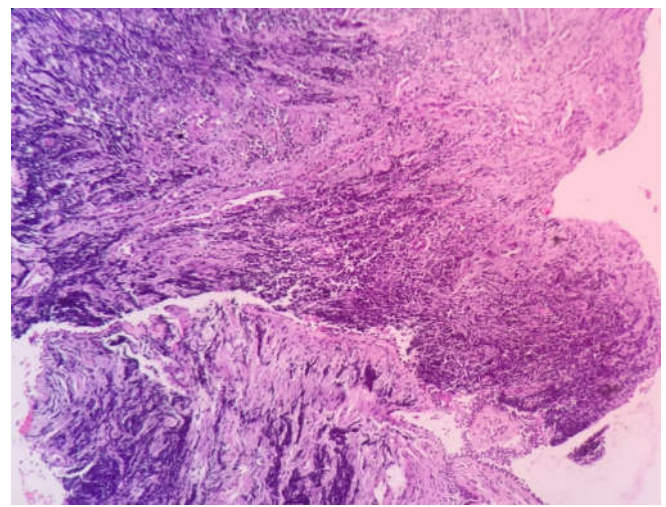
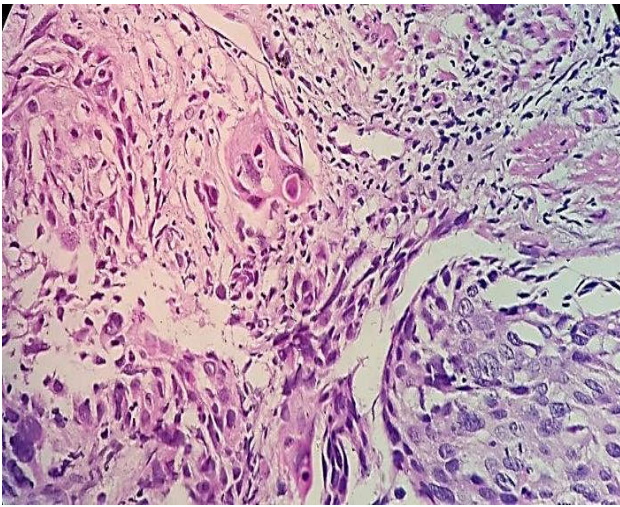


Figure 1. Squamous cell Carcinoma (individual cell Keratinization) (H&E Stain) 100x Figure 2. Small cell Carcinoma (H&E Stain) 400x

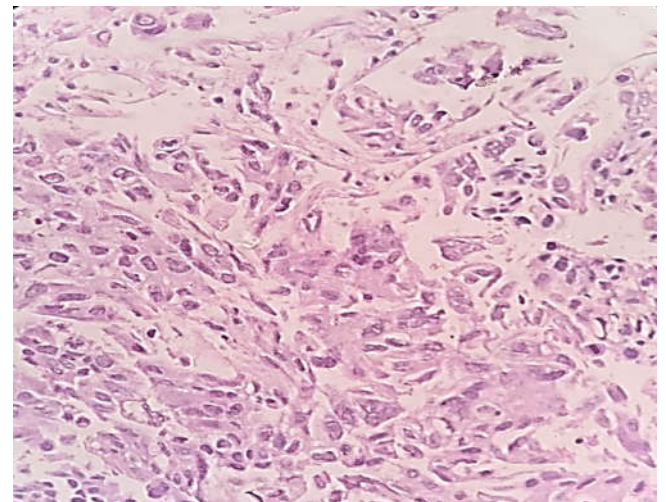
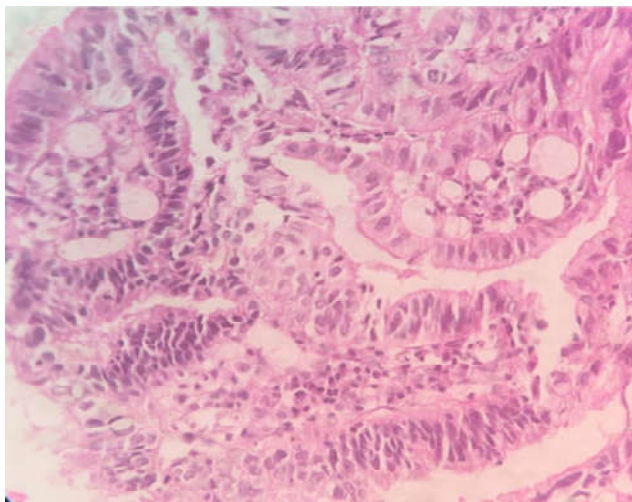


Figure 3. Adenocarcinoma (H&E Stain) 400x

Figure 4. Undifferentiated Large Cell Carcinoma (H&E Stain) 400X

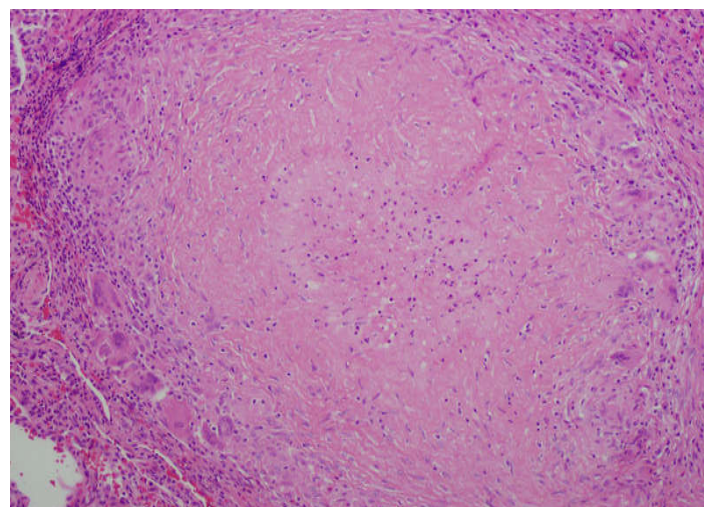


Figure 5. Granuloma in tuberculosis lung

A) Clinico pathology

Sex ratio:

Out of 130 clinically suspected cases of lung malignancies, males constituted 65.38percent (85cases) and females 34.61 percent (45cases). Male to female ratio was 1.88:1. In, 83 (84.25%) cases were diagnosed by bronchial biopsy to be suffering from lung cancer, of which 64 were males and 19 were females. The male to female ratio was 3.36:1.

b) Age distribution

The over all mean age of patients of primary lung cancer was 63.12 years with maximum number of cases seen between 61-70 years. The mean age for men was 63.23 years and for females, it was 59.44 years. The peak incidence of the disease was seen in age group of 61-70 years which constituted 40.07% per cent of all cases. The next peak was seen between 51 to 60years (25.38percent).

Agarwal et al. (2003) reported mean age of lung cancer patients as 59 years with age range of 40-78 years. The peak incidence of disease in their study was seen in the sixth decade of life.

Sheema et al. (2011) reported mean age for men as 58.33yrs and for females as 53.94 years.

Koul et al. (2010) reported mean age for men as 58.28 years and for females as 53.26 years.

Smoking risk factor

Tobacco smoking and environmental pollution have been found to be the main etiological factors for lung cancer. In the present study, out of 130 confirmed cases of lung malignancies on biopsy, there were 76 smokers and 54 non smokers. The smoker to non-smoker ratio was 1.40:1. The smoker to non-smoker ratio among males was 5.5:1, whereas among females, it was 0.097:1. Our smoker to non-smoker ratio correlates well with that of Rajasekaran et al. (1993) and Gupta et al. (2001) The low ratio of smoker to non smoker among females could be due to the fact that smoking is largely a habit of males in this part of country and usually very few females smoke.

Morphological Types of Malignancies among smokers and Non- Smokers

The two main histological sub-types of lung cancer among smokers was squamous cell carcinoma: 68.51percent and adenocarcinoma (19.27%) small cell carcinoma: 12.04 per cent. The two histological types of lung cancer are largely influenced by smoking which is evident in our study also. Rajesh Karan (1993) Agarwal (2003) in their studies also found squamous cell carcinoma to be the most common type of lung malignancies among smokers.

Summary and Conclusion

In the present study conducted on 130 bronchial biopsies (including TBB), the results are summarized as under: Out of a

total of 130 clinically suspected cases of lung cancer tumor was found in 83 cases (83/130) by biopsy. The overall mean age of patients of primary lung cancer was 63.12 years with maximum number of cases seen between 61-70years. The mean age for men was 62.23 years and for females, it was 59.34 years. The peak incidence of the disease was seen in age group of 61-70 years which constituted 32.03% percent of all cases. The next peak was seen between 51 to 60 years (28.82percent). Only 0.76% percent of cases were seen in patients less than 35 years old. Minimum age was 35year old male diagnosed as well differentiated squamous cell carcinoma, maximum age seen was 90 years.

1. Males were more common affected by lung tumors than females with a male to female ratio was 1.88:1
2. Tumor was found in the right side of lung in 58 cases (69.87%) and in the left side of lung in 25 cases (30.12%)
3. The smoker to non-smoker ratio was 1.4:1
4. The two main histological sub-types of lung cancer among smokers was squamous cell carcinoma: 65.06 percent and Adenocarcinoma: 19.27 percent).
5. The most common type of lung cancer on biopsy was squamous cell carcinoma 65.06% (54cases). The second most common type of lung cancer was Adenocarcinoma 19.27% (16 cases) including broncho-alveolar carcinoma (1 case). Small cell carcinoma 10 cases (12.04) Large cell anaplastic carcinoma were 2 cases (2.4%).
6. Diagnostic yield for endobronchial biopsy was 63.84% (83/130cases).
7. Squamous cell carcinoma (65.25%) and small cell carcinoma (12.4%) were more associated with endoscopically visible lesions than other cell types. Adenocarcinoma and (54%) and large cell carcinoma (57% were more associated with peripheral lesions.
8. Squamous cell carcinoma, Adenocarcinoma, small cell carcinoma are more common in males whereas Pleomorphic anaplastic carcinoma was seen exclusively in females.

Thus in the present study yield of diagnosis was highest with the bronchoscopic biopsies and in maximum number of cases, specific histologic diagnosis was made by biopsies only.

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